Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States

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Tenofovir Alafenamide (Genvoya, Odefsey, Descovy, TAF)

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Tenofovir alafenamide (TAF), an orally bioavailable form of tenofovir, has insufficient data on human use in pregnancy to inform a drug-associated risk determination for birth defects or miscarriage.

Animal Studies

Carcinogenicity

Because TAF is rapidly converted to tenofovir, and tenofovir exposure in rats and mice is lower after TAF administration compared to tenofovir disoproxil fumarate (TDF) administration, carcinogenicity studies were performed with TDF. Long-term oral carcinogenicity studies of tenofovir in mice and rats were carried out at 167 times (mice) and 55 times (rats) tenofovir exposure compared to that seen after TAF administration at recommended doses in humans. In female mice, liver adenomas were increased. In rats, no carcinogenic findings were observed.[1,2]

Reproduction/Fertility

Reproduction studies have been performed in rats and rabbits at exposures similar to and 53 times higher than human exposure, respectively, and revealed no evidence of impaired fertility or mating performance associated with tenofovir.[1,2]

Teratogenicity/Developmental Toxicity

No effects on early embryonic development were seen when TAF was administered to male or female rats at 62 times the human therapeutic exposure.[1-3]

Placental and Breast Milk Passage

Rat studies demonstrated secretion of tenofovir in breast milk after administration of TDF; whether TAF is present in animal milk is unknown.[1,3]

Human Studies in Pregnancy

Pharmacokinetics

No pharmacokinetic studies of TAF have been reported in pregnant women.

Placental and Breast Milk Passage

No data are available on placental or breast milk passage of TAF in humans.

Teratogenicity/Developmental Toxicity

In the Antiretroviral Pregnancy Registry, no exposures to TAF have been reported yet.[4]

Excerpt from Table 8[a]

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy
Tenofovir Alafenamide (TAF) (TAF/FTC/EVG/COBI) *Genvoya* (TAF/FTC/RPV) *Odefsey* (TAF/FTC) *Descovy*	Genvoya: • TAF 10 mg plus FTC 200 mg plus EVG 150 mg plus COBI 150 mg tablet Odefsey: • TAF 25 mg plus FTC 200 mg plus RPV 25 mg tablet Descovy: • TAF 25 mg plus FTC 200 mg tablet	Standard Adult Dose *Genvoya, Odefsey:* • 1 tablet once daily with food *Descovy:* • 1 tablet once daily with or without food • Same dose (TAF 25 mg) can be used with or without pharmacoenhancers PK in Pregnancy: • No PK studies in human pregnancy Dosing in Pregnancy: • Insufficient data to make dosing recommendation	No data on placental transfer of TAF are available. Insufficient data to assess for teratogenicity in humans. No evidence of teratogenicity in rats. Renal function should be monitored because of potential for renal toxicity.

[a] Individual antiretroviral drug dosages may need to be adjusted in renal or hepatic insufficiency (for details, see Adult and Adolescent Antiretroviral Guidelines, Appendix B, Table 7).

[b] Placental transfer categories—Mean or median cord blood/maternal delivery plasma drug ratio:

High: >0.6 **Moderate:** 0.3–0.6 **Low:** <0.3

[c] See Teratogenicity for discussion of EFV and risks in pregnancy.

Key to Acronyms: COBI = cobicistat; FTC = emtricitabine; PK = pharmacokinetic; RPV = rilpivirine; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

References

1. Tenofovir alafenamide/emtricitabine/rilpivirine (Odefsey) [package insert]. Food and Drug Administration. 2016. Available at http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/208351s000lbl.pdf.

2. Tenofovir alafenamide/evitegravir/cobicistat/emtricitabine (Genvoya) [package insert]. Food and Drug Administration. 2016. Available at http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/207561s003lbl.pdf.

3. Tenofovir alafenamide/emtrictibine (Descovy) [package insert]. Food and Drug Administration. 2016. Available at http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/208215s000lbl.pdf.

4. Antiretroviral Pregnancy Registry Steering Committee. Antiretroviral Pregnancy Registry international interim report for 1 January 1989–31 July 2015. Wilmington, NC: Registry Coordinating Center. 2015. Available at http://www.apregistry.com/.